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On Condensation Reactions of Aceanthrene Quinone: Novel Heterocycles

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Summary. It was found that aceanthrene quinone can be condensed with ethylenediamine, 1,2-diaminobenzene, 4-nitro-1,2-diaminobenzene, 1,2-diaminoanthrene quinone, and 4,5,6-triaminopyrimidine derivatives to give aceanthryleno[1,2-*b*]pyrazine and aceanthryleno[1,2-*g*]pteridine derivatives. Condensation of aceanthrene quinone with 2-aminoguanidine, semicarbazide, and thiosemicarbazide yielded aceanthryleno[1,2-*e*]triazines, condensation with 6-hydrazinopyrimidine derivatives gave 3,4-aceanthrylenopyrimido[4,5-*c*]pyridazines. Reaction of aceanthrene quinone with 2-cyanoethanoic acid hydrazide afforded 10,11-dihydro-10-oxo-aceanthryleno[1,2-*c*]pyridazine-9-carbonitrile. Treatment of aceanthrene quinone with malononitrile and hydrazine hydrate resulted in 10-aminoaceanthryleno[1,2-*c*]pyridazine-9-carbonitrile. The antibacterial effects of the prepared compounds were tested. Three of the compounds were tested against 60 cancer types.

Keywords. Condensations; Pyrazines; Triazines; Pyridazines; Antitumor activity.

Introduction

It has been shown that acenaphthene quinone and its derivatives exhibit bactericidal, antihypoxic, and fungicidal activities [1–6] and effect phospholipase A2 inhibition [7]. Acenaphthene quinone hydrogensulfite exerts a narcotic effect on mice and inhibits the growth of transplanted tumors [3]. The condensation product of acenaphthenequinone with 2,3-diaminopyrazine provokes ataxia by lowering the central nervous system activity [6]. Although there is an abundance of reports dealing with the chemistry of acenaphthene quinone, very little is known about the reactions of benzoacenaphthene quinone (aceanthrene quinone) and its derivatives. Moreover, aceanthrene quinone derivatives have been extensively utilized as intermediates for the synthesis of fused aceanthrenes of potential biological activity [8, 9]. In connection with these finding and our interest in the synthetic potential of fused nitrogen heterocyclic compounds [10, 11], we report on the synthesis of fused aceanthrene systems with the aim of studying their utility as pharmacological agents.

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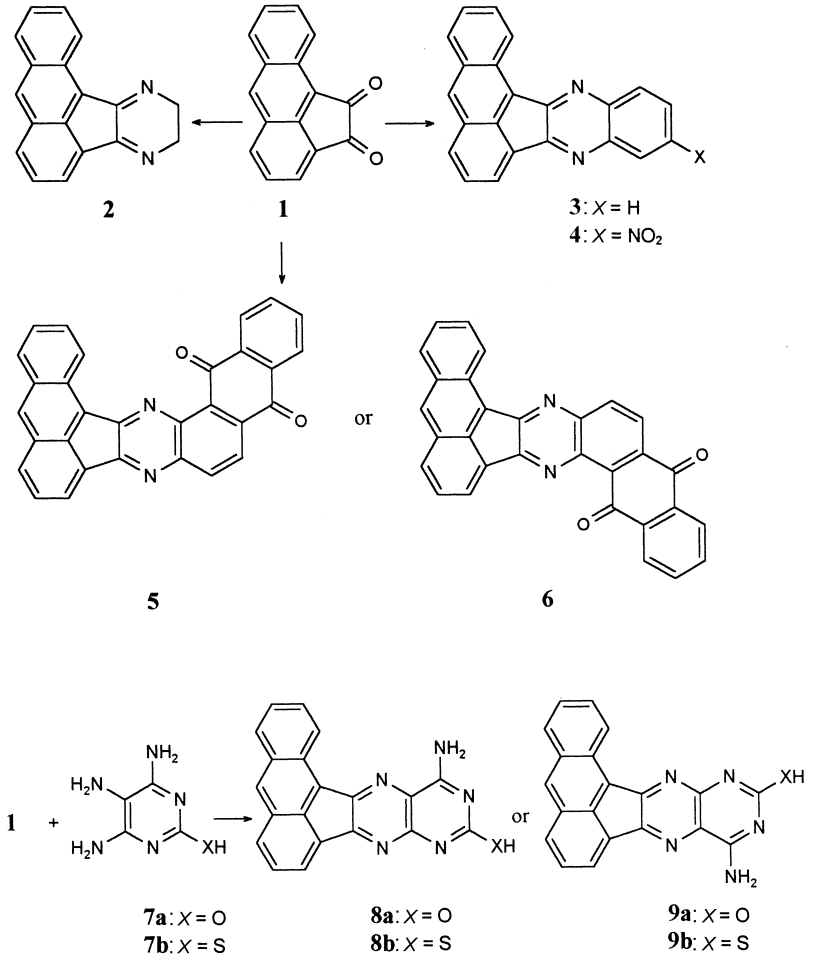
Results and Discussion

The condensation of 1,2-diketone **1** with aliphatic diamines was carried out as described by *Chiodini* [12] to give fused pyrazine derivatives in good yield. Thus, treatment of **1** with ethylenediamine at reflux temperature gave 10,11-dihydroaceanthryleno[1,2-*b*]pyrazine (**2**). The reaction of **1** with the aromatic diamines 1,2-diaminobenzene, 4-nitro-1,2-diaminobenzene, and 1,2-diaminoanthraquinone in acidic medium under reflux yielded the aceanthryleno[1,2-*b*]quinoxaline derivatives **3**–**5** (Scheme 1).

With respect to structural details, Hyperchem calculations on **5** and **6** were by no means indicative since the two heats of formation (92.06 and 92.02) were virtually identical. Thus, there will be no thermodynamic reason for the favoured formation of either one. In addition, the calculated dipole moments did not differ significantly (4.07 and 4.18 D). The relative reactivities of the two carbonyl groups of **1** as well as those of the two amino groups in 1,2-diaminoanthrene quinone determine the regioselectivity of the reaction. Accordingly, nucleophilic attack of the more basic nitrogen atom to the carbonyl group at position 2 (which is more

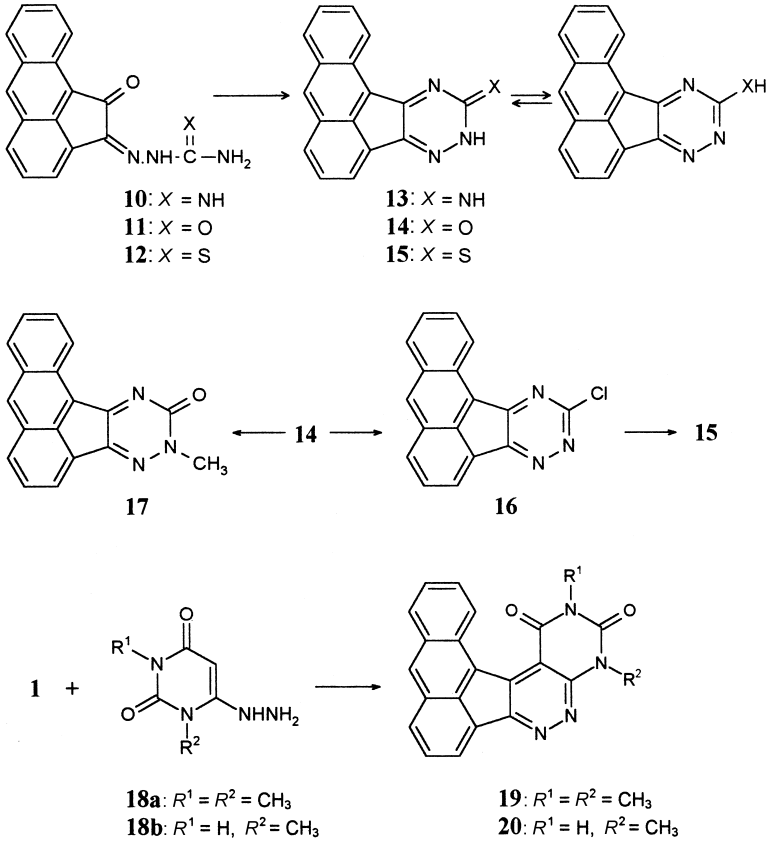


Scheme 1

reactive [8, 13, 14]) of the aceanthrene quinone followed by cyclization with elimination of water will give **5**. This type of regioselectivity agrees with literature [8, 13–17].

Condensation of **1** with 4,5,6-triaminopyrimidine derivatives **7a** and **7b** [18] in acetic acid under reflux afforded the corresponding cyclic aceanthryleno[1,2-*g*]pteridine derivatives **8a**,**b** and **9a**,**b**. The condensation first links the more basic amino group at position 5 of the pyrimidine derivatives **7** [18] with the carbonyl group at position 2 (which is more reactive [8, 14]) in the aceanthrene quinone, followed by cyclization with elimination of water.

In continuation of our efforts directed towards the synthesis of bi- and tricyclic systems containing the 1,2,4-triazine subunit, we tried to synthesize the aceanthryleno[1,2-*e*]triazine system employing **1** as the starting material. Treatment of **1** with aminoguanidine bicarbonate in pyridine under reflux readily afforded 11-aminoaceanthryleno[1,2-*e*]triazine (**13**), probably *via* the intermediate guanylhydrazone **10** which was not isolated. Similarly, the reaction of **1** with semicarbazide or thio-semicarbazide reflux gave the corresponding cyclic products **14** and **15**. Treatment of **14** with $POCl_3$ under reflux afforded 11-chloroaceanthryleno[1,2-*e*]triazine **16** which reacted with thiourea to give **15**. Furthermore, **14** was treated with methyl iodide in aqueous KOH at room temperature to give N-methyl-aceanthryleno[1,2-*e*]triazin-3-one (**17**).

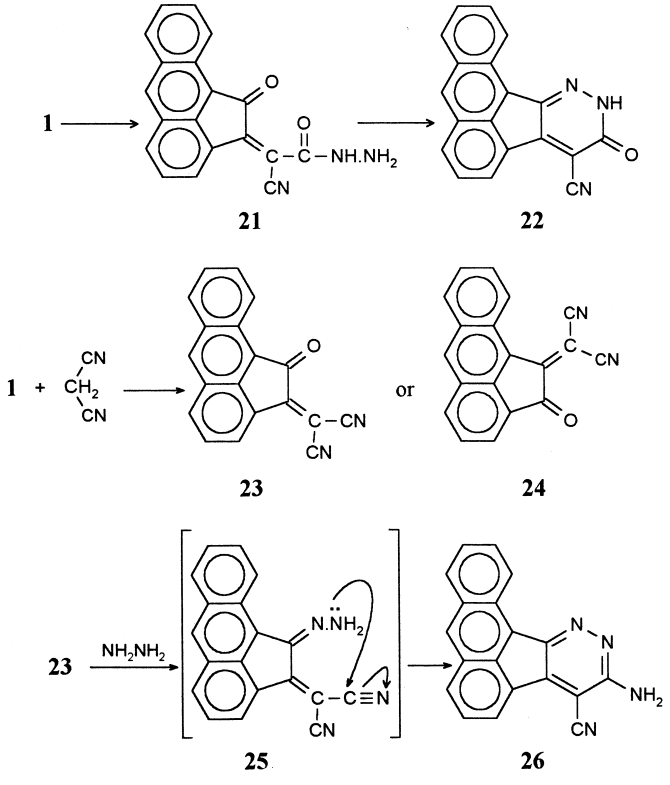


Scheme 2

The reaction of **1** with the 6-hydrazinouracil derivatives **18a**,**b** in refluxing acetic acid resulted in 3,4-aceanthryleno-5,7-dioxotetrahydro-6,8-dimethylpyrimido[4,5-*c*]pyridazine (**19**) and 3,4-aceanthryleno-5,7-dioxotetrahydro-8-methylpyrimido[4,5-*c*]pyridazine (**20**). The condensation was always immediately followed by cyclization; attempts to isolate the condensed products were unsuccessful. When **1** was treated with 2-cyanoethanoic acid hydrazide it afforded **21**, which underwent cyclization in aqueous KOH at reflux temperature to afford 10,11-dihydro-10-oxo-aceanthryleno[1,2-*c*]pyridazine-9-carbonitrile (**22**).

Treatment of **1** with malononitrile in dimethylformamide at reflux afforded 2-(dicyanomethylene)-aceanthren-1-one (**23**) and not **24**; this was rationalized by Gaussian 98 calculations which showed that **23** is more stable than **24** by 25.9 $kJ \cdot mol^{-1}$. When **23** was reacted with hydrazine hydrate, 10-aminoaceanthryleno[1,2-*c*]pyridazine-9-carbonitrile (**26**) was obtained. A mechanism is proposed to account for the formation of this product. First, nucleophilic attack of the basic nitrogen atom on the carbonyl group in position 1 with elimination of water rather than substitution of the cyano group will give **25**. Then, cyclization affords **26**. The structure of all new compounds were confirmed by elemental analysis and spectroscopic data.

Compounds **1**–**4**, **14**, and **15** were tested for antimicrobial activity using the agar diffusion method [19] against representatives of *Gram*-positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*) and *Gram*-negative bacteria



Scheme 3

Table 1. Growth of cancer cell lines in presence of **4**, **5**, and **23**

Panel/Cell Line	% Growth in presence of **4** lg c (mg/cm^3)		% Growth in presence of **5** lg c (mg/cm^3)		% Growth in presence of **23** lg c (mg/cm^3)	
	−5.0	−4.0	−5.0	−4.0	−5.0	−4.0
Leukemia						
CCRF-CEM	29	26	32	19	107	56
HL-60(TB)	59	16	60	23	103	39
MOLT-4	16	77	54	49	111	39
RPMI-8226	24	87	79	43	98	65
SR	22	45	44	34	88	24
Non-small cell lung cancer						
A549/ATCC	83	17	101	30	104	91
NCI-H226	42	52	101	26	82	53
NCI-H23	18	−28	98	25	83	55
NCI-H322M	81	37	91	52	93	57
NCI-H460	56	14	77	12	118	94
Colon cancer						
COLO 205	87	80	119	46	103	81
HCC-2998	80	22	109	50	122	122
HCT-116	10	15	33	13	93	43
HCT-15	36	4	77	23	135	94
HT29	31	4	70	7	96	51
KM12	12	1	54	9	88	38
SW-620	22	25	68	38	101	53
CNS cancer						
SNB-19	27	−30	76	11	81	52
U251	29	−16	78	18	103	57
Melanoma						
LOX IMVI	−33	−40	61	8	95	52
M14	73	−6	78	13	104	91
SK-MEL-2	92	−4	91	14	88	49
SK-MEL-28	81	44	104	46	107	47
SK-MEL-5	71	26	95	5	97	84
UACC-257	58	18	110	65	105	88
UACC-62	68	−33	84	20	87	54
Ovarian cancer						
IGROV1	−7	−40	27	−25	79	31
OVCAR-3	96	−2	97	24	93	80
OVCAR-4	63	31	103	50	181	154
OVCAR-5	86	40	99	53	113	103
SK-OV-3	85	−28	96	40	111	83
Renal cancer						
786-0	23	6	70	8	87	19
A498	−48	−51	87	52	109	102

(*continued*)

Table 1 (*continued*)

Panel/Cell Line	% Growth in presence of **4** lg c (mg/cm^3)		% Growth in presence of **5** lg c (mg/cm^3)		% Growth in presence of **23** lg c (mg/cm^3)	
	−5.0	−4.0	−5.0	−4.0	−5.0	−4.0
ACHN	50	1	76	12	79	28
CAKI-1	14	−50	78	11	92	83
SN12C	51	4	93	12	102	85
Prostate cancer						
PC-3	45	0	88	20	67	44
DU-145	95	22	78	−17	100	74
Breast cancer						
MDA-MB-231/ATCC	77	−16	97	41	77	56
HS 578T	26	−24	31	−40	108	−8
MDA-MB-435	92	−17	97	−49	108	71
MDA-N	52	−24	90	3	91	64
BT-549	8	−24	90	46	86	74

(*E. coli* and *Pseudomonas aeruginosa*). Compounds **1**–**4** (at a concentration of 0.06 mg · cm^{-3}) showed good inhibition zones of *E. coli*. Only **2** showed very good inhibition zones of *Bacillus subtilis*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Compared with streptomycin, these compounds exhibited similar or even better inhibition results.

The effects of **4**, **5**, and **23** were tested against several cancer lines (Table 1). The cell panel consisting of 60 lines was tested at a minimum of five concentrations at 10-fold dilutions. A 48 hour continuous drug exposure protocol was used, and a sulforhodamine B (*SRB*) protein assay was used to estimate cell viability or growth. The results presented in Table 1 show that depending on the functional group on the aceanthrene ring a varied growth depression is observed. Thus, the cyano group in **23** is much less effective as compared to the pyrazine derivatives **4** and **5**.

Experimental

Melting points were measured on a Kofler hot stage microscope (Reichert, Vienna) and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker DPX 200 spectrometer at 200 MHz (^{1}H); chemical shifts are given in δ units relative to internal *TMS* at 295 K. IR spectra were obtained on a Biorad FT-IR-45 instrument. All experiments were carried out with exclusion of moisture. For all new compounds satisfactory elemental analyses were obtained. Aceanthrene quinone (**1**) and 6-hydrazinopyrimidines (**18a**,**b**) were prepared as previously described [8, 19].

Reaction of **1** *with diamine derivatives; general procedure*

A mixture of 0.26 g **1** (1 mmol) and 1.0 to 1.5 mmol of the appropriate diamine derivatives (ethylenediamine, phenylenediamine, 1,2-diamino-4-nitrobenzene, 1,2-diaminoanthraquinone, 4,5,6-triamino-2-hydroxy-pyrimidine, 4,5,6-triamino-2-thiopyrimidine) in 50 cm^3 acetic acid was heated under reflux for 3–5 h. The solvent was removed under reduced pressure and the solid product was filtered off and recrystallized from a suitable solvent to give the products **2**–**6**, **9a**, and **9b**.

10,11-Dihydroaceanthryleno[1,2-b]pyrazine (**2**; $C_{18}H_{12}N_2$)

Prepared from **1** and ethylenediamine (1.5 mmol); crystallization from petroleum ether (60–80); yellow crystals; yield: 2.13 g (83%); m.p.: 138–139°C; IR (KBr): $\nu = 3010$, 2985, 1660, 1620–1490 cm^{-1}; ^1H NMR ($CDCl_3$, δ, 200 MHz): 4.0 (m, $2CH_2$), 7.56–7.71 (m, $3H_{ar}$), 7.72 (d, $J = 6.6$ Hz, $1H_{ar}$), 8.06–8.14 (m, $2H_{ar}$), 8.54 (s, $1H_{ar}$), 9.05–9.09 (d, $J = 8.2$, $1H_{ar}$) ppm.

Aceanthryleno[1,2-b]quinoxaline (**3**; $C_{22}H_{12}N_2$)

Prepared from **1** and 1,2-diaminobenzene (1 mmol); crystallization from pyridine; orange crystals; yield: 2.23 g (75%); m.p.: 245°C; IR (KBr): $\nu = 3030$, 1622, 1655, 1625–1480 cm^{-1}; ^1H NMR ($CDCl_3$, δ, 200 MHz): 7.51 (t, $1H_{ar}$), 7.70 (m, $4H_{ar}$), 8.05–8.20 (m, $4H_{ar}$), 8.35 (d, $J = 6.8$ Hz, $1H_{ar}$), 8.50 (s, $1H_{ar}$), 9.45 (d, $J = 8.9$ Hz, $1H_{ar}$) ppm.

11-Nitro-aceanthryleno[1,2-b]quinoxaline (**4**; $C_{22}H_{11}N_3O_2$)

Prepared from **1** and 1,2-diamino-4-nitro-benzene (1 mmol); crystallization from benzene; brownish red crystals; yield: 2.37 g (68%); m.p.: 280°C (dec.); IR (KBr): $\nu = 3108$, 1657, 1622, 1610, 1580, 1522, 1482 cm^{-1}.

Aceanthryleno[1,2-b]pyrazino[5,6:1,2]anthraquinone (**5**; $C_{30}H_{14}N_2O_2$)

Prepared from **1** (1 mmol) and 1,2-diaminoanthraquinone (1 mmol); crystallization from acetic acid; brown crystals; yield: 1.52 g (35%); m.p.: 278–280°C; IR (KBr): $\nu = 3010$, 1625, 1615, 1568, 1520, 1480 cm^{-1}; ^1H NMR ($CDCl_3$/*DMSO*-d_6, δ, 200 MHz): 7.50 (m, $3H_{ar}$), 7.62–7.84 (m, $3H_{ar}$), 8.27 (m, $5H_{ar}$), 8.55 (m, $3H_{ar}$) ppm.

10-Amino-13-hydroxy-aceanthryleno[1,2-g]pteridine (**9a**; $C_{20}H_{11}N_5O$)

Prepared from **1** (1 mmol) and 4,5,6-triaminopyrimidin-2-one (1 mmol); crystallization from EtOH; orange crystals; yield: 1.35 g (40%); m.p.: >360°C; IR (KBr): $\nu = 3441$, 3363, 3236, 1670, 1619, 1599, 1585, 1482 cm^{-1}; ^1H NMR (*DMSO*-d_6, δ, 200 MHz): 6.50 (br, NH_2), 7.55–7.70 (m, $3H_{ar}$), 7.82 (d, $J = 6.7$ Hz, $1H_{ar}$), 8.06–8.13 (m, $2H_{ar}$), 8.55 (s, $1H_{ar}$), 9.10 (d, $J = 8.5$ Hz, $1H_{ar}$), 11.80 (br, NH) ppm.

10-Amino-13-mercapto-aceanthryleno[1,2-g]pteridine (**9b**; $C_{20}H_{11}N_5S$)

Prepared from **1** (1 mmol) and 4,5,6-triaminopyrimidine-2-thione (1 mmol); crystallization from EtOH; orange crystals; yield: 1.17 g (33%); m.p.: 230–232°C; IR (KBr): $\nu = 3448$, 3350, 3110, 3040, 1630, 1622, 1580, 1518, 1225 cm^{-1}.

11-Aminoaceanthryleno[1,2-e]triazine (**13**; $C_{17}H_{10}N_4$)

A mixture of **1** (1 mmol), aminoguanidine bicarbonate (1 mmol), and 50 cm^3 dry pyridine was refluxed with stirring for 5 h. After cooling, the reaction mixture was poured into 25 cm^3 H_2O and 5 cm^3 30% HCl. The precipitated product was filtered, dried, and crystallized from benzene.

Brown crystals; yield: 1.75 g (65%); m.p.: 180°C; IR (KBr): $\nu = 3460$, 3380, 3110, 3040, 1630, 1622, 1580, 1500 cm^{-1}; ^1H NMR ($CDCl_3$, δ, 200 MHz): 7.70–7.90 (m, $3H_{ar}$), 8.05–8.20 (m, $2H_{ar}$), 8.35 (d, $J = 8.3$ Hz, $1H_{ar}$), 8.90 (s, $1H_{ar}$), 9.15 (d, $J = 8.5$ Hz, $1H_{ar}$) ppm.

Reaction of **1** *with semicarbazide and thiosemicarbazide; general procedure*

A mixture of 0.30 g **1** (1.2 mmol), 20 cm^3 toluene, 1.2 mmol semicarbazide hydrochloride or thiosemicarbazide, and 5 drops of acetic acid was refluxed with stirring for 5 h. After cooling, the solid was collected by suction and crystallized from a suitable solvent to yield **14** and **15**.

11-Hydroxyaceanthryleno[1,2-e]triazine (**14**; $C_{17}H_9N_3O$)

Crystallized from *DMF*/H_2O; faint brown crystals; yield: 1.17 g (43%); m.p.: 221°C; IR (KBr): $\nu = 3446$, 3037, 1670, 1628, 1580, 1486 cm^{-1}; ^1H NMR (*DMSO*-d_6/D_2O, δ, 200 MHz): 7.70–8.00 (m, $4H_{ar}$), 8.10–8.25 (m, $2H_{ar}$), 8.90–9.15 (m, $2H_{ar}$) ppm.

11-Mercaptoaceanthryleno[1,2-e]triazine (**15**; $C_{17}H_9N_3S$)

Crystallized from toluene; faint brown crystals; yield: 1.29 g (45%); m.p.: 238–239°C; IR (KBr): $\nu = 3420$, 3031, 1632, 1610, 1580, 1500, 1208 cm^{-1}. ^1H NMR (*DMSO*-d_6, δ, 200 MHz): 7.23–7.90 (m, $4H_{ar}$), 8.10 (m, $2H_{ar}$), 8.90 (s, $1H_{ar}$), 9.10 (d, $J = 8.6$ Hz, $1H_{ar}$), 11.80 (br, NH) ppm.

11-Chloroaceanthryleno[1,2-e]triazine (**16**; $C_{17}H_8N_3Cl$)

A mixture of 0.27 g **14** (1 mmol) and 5 cm^3 $POCl_3$ was refluxed for 3 h at 140°C. The excess of solvent was removed under reduced pressure, and the residue was poured on crushed ice with vigorous stirring. The brown solid obtained was washed with 2% KOH to remove unreacted parent compound and crystallized from EtOH to give faintly brown crystals.

Yield: 1.30 g (45%); m.p.: >250°C; IR (KBr): $\nu = 3047$, 1630, 1600, 1578, 1510 cm^{-1}; ^1H NMR (*DMSO*-d_6, δ, 200 MHz): 7.50–7.60 (m, $4H_{ar}$), 7.70 (d, $J = 6.7$ Hz, $1H_{ar}$), 7.80 (d, $J = 7.5$ Hz, $2H_{ar}$), 8.10 (d, $J = 8.3$ Hz, $1H_{ar}$), 8.60 (s, $1H_{ar}$), 9.10 (d, $J = 8.7$ Hz, $1H_{ar}$) ppm.

10,11-Dihydro-10-methylaceanthryleno[1,2-e]triazine (**17**; $C_{18}H_{11}N_3O$)

A solution of 0.27 g **16** (1 mmol) in 3 cm^3 KOH (5%) was stirred overnight with 0.2 cm^3 CH_3I at room temperature. The precipitate separated was washed with H_2O and recrystallized from *DMF*/H_2O to produce red crystals.

Yield: 1.71 g (60%); m.p.: 160°C; IR (KBr): $\nu = 3045$, 2987, 1685, 1621, 1583, 1494 cm^{-1}; ^1H NMR ($CDCl_3$, δ, 200 MHz): 3.35 (s, CH_3), 7.60 (m, $3H_{ar}$), 7.72 (d, $J = 6.8$ Hz, $1H_{ar}$), 8.06 (m, $2H_{ar}$), 8.54 (s, $1H_{ar}$), 9.10 (d, $J = 8.7$ Hz, $1H_{ar}$) ppm.

3,4-Aceanthrylenopyrimido[4,5-c]pyridazine derivatives **19** and **20***; general procedure*

A mixture of 0.4 mmol **18a** or **18b** with 0.10 g **1** (0.4 mmol) in 10 cm^3 acetic acid was refluxed for 5 h and allowed to stand overnight at room temperature. The resulting precipitate was collected, washed with cold H_2O, and recrystallized from EtOH-*DMF* to yield **19** and **20**.

3,4-Aceanthryleno-5,7-dioxotetrahydro-6,8-dimethylpyrimido[4,5-c]pyridazine (**19**; $C_{22}H_{14}N_4O_2$)

Yellow crystals; yield: 2.02 g (55%); m.p.: >300°C; IR (KBr): $\nu = 3046$, 2988, 1700, 1682, 1618, 1522, 1485 cm^{-1}; ^1H NMR (*DMSO*-d_6, δ, 200 MHz): 3.80 (s, CH_3), 4.10 (s, CH_3), 7.65–8.05 (m, $4H_{ar}$), 8.32 (d, $J = 8.1$ Hz, $2H_{ar}$), 8.90 (d, $J = 8.7$ Hz, $1H_{ar}$), 9.10 (s, $1H_{ar}$) ppm.

3,4-Aceanthryleno-5,7-dioxotetrahydro-8-methylpyrimido[4,5-c]pyridazine (**20**; $C_{21}H_{12}N_4O_2$)

Orange yellow crystals; yield: 2.12 g (60%); m.p.: >300°C; IR (KBr): $\nu = 3270$ br, 3046, 1708, 1776, 1612, 1585, 1483 cm^{-1}; ^1H NMR (*DMSO*-d_6, δ, 200 MHz): 3.75 (s, CH_3), 7.65–7.95 (m, $3H_{ar}$), 8.00 (d, $J = 8.1$ Hz, $1H_{ar}$), 8.25–8.43 (m, $2H_{ar}$), 8.90 (d, $J = 8.7$ Hz, $1H_{ar}$), 9.10 (s, $1H_{ar}$), 12.95 (br, NH) ppm.

2-(Cyanoethylenoyl hydrazine)-aceanthren-1-one (**21**; $C_{19}H_{11}N_3O_2$)

A mixture of 0.12 g **1** (0.5 mmol), 0.12 g 2-cyanoethanoic acid hydrazide (0.5 mmol), and 20 cm^3 acetic acid was heated under reflux for 2 h. The yellow solid obtained was filtered off and recrystallization from ethyl acetate to give **21**.

Yield: 2.50 g (80%); m.p.: 248°C; IR (KBr): $\nu = 3446$, 3350, 3138, 3046, 2225, 1710, 1686, 1628, 1618 cm^{-1}; ^1H NMR (*DMSO*-d_6, δ, 200 MHz): 4.20 (br, NH_2), 7.75–7.90 (m, $3H_{ar}$), 8.25 (m, $3H_{ar}$), 8.61 (d, $J = 8.5$ Hz, $1H_{ar}$), 9.10 (s, $1H_{ar}$), 11.80 (br, NH) ppm.

10,11-Dihydro-10-oxo-aceanthryleno[1,2-c]pyridazine-9-carbonitrile (**22**; $C_{19}H_9N_3O$)

A suspension of 0.16 g **21** (0.5 mmol) in 10 cm^3 KOH 5% was refluxed for 2 h, cooled, and filtered. The filtrate was neutralized with 5 *N* HCl and cooled. The brown precipitate separated was washed with H_2O and recrystallized from *DMF*/H_2O to give brown crystals.

Yield: 1.48 g (50%); m.p.: >290°C; IR (KBr): $\nu = 3399$, 3046, 2258, 1684, 1616, 1588, 1500 cm^{-1}; ^1H NMR (*DMSO*-d_6, δ, 200 MHz): 7.70–7.90 (m, $3H_{ar}$), 8.21–8.63 (m, $3H_{ar}$), 9.10 (s, $1H_{ar}$), 9.42 (d, $J = 9.0$ Hz, $1H_{ar}$), 13.25 (br, NH) ppm.

2-(Dicyanomethylene)-aceanthren-1-one (**23**; $C_{19}H_8N_2O$)

A mixture of 0.12 g **1** (0.5 mmol) and 0.33 g malononitrile (0.5 mmol), 10 cm^3 toluene, and 1 cm^3 acetic acid was refluxed for 2 h. Workup and crystallization from *DMF* gave brown crystals.

Yield: 2.58 g (92%); m.p.: 392°C; IR (KBr): $\nu = 3042$, 2226, 1689, 1596, 1522, 1454 cm^{-1}; ^1H NMR (*DMSO*-d_6, δ, 200 MHz): 7.40–8.50 (m, $6H_{ar}$), 9.0 (d, $J = 8.9$ Hz, $1H_{ar}$), 9.15 (s, $1H_{ar}$) ppm; MS: $m/z = 280$ (M^+; 100%), 252 (M^+-CO; 15%), 225 (M^+-(CO + HCN); 20%), 113 (16%).

10-Aminoaceanthryleno[1,2-c]pyridazine-9-carbonitrile (**26**; $C_{19}H_{10}N_4$)

A suspension of 0.20 g **23** (0.86 mmol) and 0.05 cm^3 hydrazine hydrate (1 mmol) in 8 cm^3 benzene was heated under reflux for 2 h, cooled, filtered, and dried. Crystallization from EtOH gave faintly brown crystals.

Yield: 1.26 g (43%); m.p.: 191–195°C; IR (KBr): $\nu = 3676$, 3177, 3040, 2198, 1628, 1616, 1582, 1456 cm^{-1}; ^1H NMR (*DMSO*-d_6, δ, 200 MHz): 7.50–7.79 (m, $4H_{ar}$), 7.90–8.22 (d, $J = 6.8$ Hz, $2H_{ar}$), 8.50 (d, $J = 8.5$ Hz, $1H_{ar}$), 9.10 (s, $1H_{ar}$), 11.20 (br, NH_2) ppm.

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